Chemico-Biological Interactions 308 (2019) 110–112

Contents lists available at ScienceDirect

Chemico-Biological Interactions

journal homepage: www.elsevier.com/locate/chembioint

EPA adopts LNT: New historical perspectives

Edward J. Calabrese

Department of Environmental Health Sciences, Morrill I, N344, University of Massachusetts, Amherst, MA, 01003, USA

ARTICLE INFO

Keywords:
LNT
Cancer risk assessment
Dose response
Threshold dose response
Somatic mutation
Environmental protection agency

ABSTRACT

This paper provides an historical assessment of how the linear non-threshold (LNT) model became adopted as policy by the United States Environmental Protection Agency (US EPA) in 1975 [1] and how prior United States National Academy of Sciences (US NAS) radiation advisory panels may have affected this EPA decision. The paper highlights a generally unrecognized set of recommendations of the 1960 Biological Effect of Atomic Radiation [2] Genetics and Medical/Pathology Panels that did not support LNT for cancer risk assessment due to their judgements of its scientific limitations and unacceptable uncertainties. These convergent, independent and high profile recommendations were not promoted by the sponsors (i.e., Rockefeller Foundation and the NAS), and were ignored by the media, Congress and the scientific community in contrast to the vast attention directed to the linearity recommendation for germ cell mutation by the BEAR Genetics Panel in 1956 [3,4]. The subsequent Biological Effects of Ionizing Radiation (BEIR) I Committee (1972) [5] report ignored these BEAR Panel (1960) [2] recommendations, only commenting on the BEAR 1956 linearity supporting recommendation [3,4]. These actions are documented and assessed for how they influenced why and how EPA adopted linearity for cancer risk assessment based on the BEIR I report.

1. Introduction

In 1956, the US National Academy of Sciences (NAS) Biological Effects of Atomic Radiation (BEAR) I Genetics Panel [3,4] recommended that risk assessment for ionizing radiation for germ cell mutation be switched from a threshold to a linear dose response. This was a precipitous moment in risk assessment history that was long anticipated and highly publicized (e.g. it became a prominent paper in the journal *Science*, front page stories in the *New York Times* and *Washington Post* and other major outlets with the report sent to all public libraries in the United States) [6]. The NAS BEAR I Genetics Panel was considered the 1950's equivalent of a genetics "Dream Team", having great influence and standing within the scientific, legislative, regulatory, news media and general public communities. Their report was followed by Congressional Hearings in 1957 [7,8] and influenced advisory groups such as the National Council on Radiation Protection and Measurements (NCRPM) to adopt a linear dose response for cancer risk assessment in December 1958 [9], which, itself, proved to be a similarly major development [8,10].

2. NCRPM cancer risk assessment linearity recommendation

The December 1958 NCRPM position [9] was based on the assumption that radiation induced genetic damage is "completely cumulative and that the effect is independent of the rate at which the radiation is delivered." [11]. This statement embraces the geneticist mantra of the 1950s and the position of the 1956 NAS BEAR Genetics Panel Report [3,4]. However, in contrast to the scientific beliefs of the 1956 BEAR Genetics Panel [3,4], the 1960 NCRPM [11] statement did not accept these assumptions and conclusions as established facts; the NCRPM specifically stated that they were adopted as prudent public health policy, reflecting in effect a Precautionary Principle. The timing of the 1958 NCRPM policy meeting (Dec. 29/30, 1958) [9] was remarkable being about two weeks after the seminal publication of Russell et al. in the journal *Science* on December 19th, 1958 [12] demonstrating that radiation-induced mutation frequency was explained by dose rate, not total dose, and that such mutations could be readily repaired. There has been no record yet obtained that clarifies why the decision to adopt a linear dose response policy by the NCRPM was not affected by the Russell et al. [12] findings since James Crow and Edwin B Lewis, both prominent figures in the radiation geneticist community, were members of the NCRPM Committee. That is, why didn't NCRPM delay this decision, pending a review of the Russell findings [12]?

Of particular relevance to the LNT issue is that the 1956 BEAR Medical/Pathology Panel [4,13], which met concurrently with the BEAR Genetics Panel, offered a different perspective/evaluation of ionizing radiation induced mutation and its relationship to cancer as did the Genetics Panel. The Medical/Pathology Panel downplayed and even

E-mail address: edwardc@schoolph.umass.edu.

https://doi.org/10.1016/j.cbi.2019.05.027
Received 25 April 2019; Received in revised form 13 May 2019; Accepted 15 May 2019
Available online 17 May 2019
0009-2797/

questioned the role of somatic mutation in cancer as seen in the following comment. "If somatic mutation is a necessary part of the induction of cancer, it would seem to play a minor role." (page 62, right column) [13]. They also noted that at the permissible dose level for germ cells as recommended for large populations by the Genetics Panel "there would be no demonstrable somatic effect .... " (page 62, right column) [13]. This conclusion was supportive of a threshold dose response for both somatic mutation and cancer. This perspective was not highlighted with the publication of the 1956 BEAR Report in June [4], nor was it even contrasted with the striking linearity recommendation of the Genetics Panel in press releases or news media stories.

Since the two Panels had differing charges and different scientific education/training, it is not surprising that they viewed the issue of mutation differently. These differing perspectives had long been apparent during high-level advisory committees where the medical perspective had been dominant due to the composition of the committee memberships. In fact, a principal tactic of the Rockefeller Foundation (RF), which funded the NAS BEAR activities, was to give the radiation geneticists a voice of their own, thereby quietly ensuring their (i.e. RF) goal that the LNT perspective would become policy. This suggestion is supported by the fact that Chairman Weaver and President Bronk selected geneticists that strongly supported LNT. This would prove to be a major stealth-like strategic decision by a non-governmental funding entity that changed the course of national and international governmental cancer risk assessment history. The action was greatly facilitated by the fact the President of the Rockefeller Institute for Medical Sciences (later renamed Rockefeller University) and the President of the US National Academy of Sciences was the same person, Dr. Detlev Bronk.

The NCRPM Committee (1958) (cited in 1960) [11] opted to use the linearity concept of the Genetics Panel for their recommendation for cancer risk assessment, even though cancer risk was in the domain of the Medical/Pathology Panel while germ cell risk was the focus of the Genetics panel.

The 1956 BEAR Genetics Panel would continue to function until 1964. The NAS Biological Effects of Ionizing Radiation (BEIR) would be re-formed in 1970 to address the issue of nuclear power, with James Crow, who had served on the previous BEAR Panels while chairing its final activities, becoming Chair of BEIR I, Genetics Subcommittee.

While vast attention was given to the 1956 Genetics Panel groundbreaking report, no such attention was given to their continuing efforts to address new scientific developments and concerns. Yet, the BEAR 1960 [2] report contained similarly significant independent recommendations by both the Genetics and Medical/Pathology Panels on predicting cancer risks in humans from low doses of ionizing radiation.

3. BEAR 1960 Genetics and Pathology Panels LNT recommednations

The recommendations for cancer risk assessment by the two Panels might have caught those who studied their 1956 reports by surprise. The two Panels arrived at the same conclusion that there were too many uncertainties and that cancer risk estimates could not be reliably done. In the words of the 1960 Medical/Pathology Panel [2]: "... the Committee does not consider it justifiable to predict human tumor incidences from small radiation doses based on extrapolation from the observed incidences following high dosage" (page 32). In the case of the 1960 Genetics Panel [2]: "We cannot say with any assurance whether the dose-response curve for induction of malignant disease is linear or non-linear at low levels." (page 10).

The converging statements of the two Panels in 1960 [2] represented a fundamental conclusion with major policy implications. It also represented major policy changes by both Panels from their positions in 1956. In the case of the Medicine/Pathology Panel there was a movement from strong support for a threshold model toward uncertainty. In the case of the Genetics Panel, their support for linearity for radiation induced gene mutation did not apply to radiation induced cancer risk assessment even though the mechanistic driver for many in the genetics community at this time was mutation. However, despite the importance of these conclusions, there was no fanfare, front page stories, reports sent to all public libraries, publications in *Science* or Congressional Hearings. The BEAR Genetics and Medical/Pathology Panel (1960) [2] activities seemed to have been intentionally relegated to secondary status, becoming a silent report. In subtle ways both Panel reports morphed to a position that supported the Precautionary Principle recommendation for cancer risk assessment by the NCRPM (1960) [11]. In retrospect, this was precisely what happened.

These joint 1960 BEAR Panel recommendations (i.e., Genetics and Medicine/Pathology) were ignored for the next 10 years, even by the Biological Effects of Ionizing Radiation (BEIR) I Genetics Subcommittee Report published in 1972 [5]. This 1972 BEIR report commented in detail on the 1956 Genetics Panel report, addressing significant changes since 1956, the most important being that of William Russell on dose rate, which the 1956 Genetics Panel admittedly got wrong. This is particularly important since the geneticist mantra was based on the belief that radiation induced mutation was not affected by dose rate and repair did not occur. This mistake was significant since the new Russell findings suggested the possibility of thresholds for mutation as well as for cancer risks. The Russell findings also signaled the existence of DNA repair, a suggestion that Edgar Altenburg shared with Hermann Muller within a few days of the Russell publication in letter correspondence [14].

While the BEIR I Genetics Subcommittee would struggle with the dose rate issue in its 1972 report [5], it is remarkable that this Genetics Subcommittee failed to address/comment on the 1960 BEAR Genetics and Medical/Pathology Panel [2] reports that high to low dose extrapolation for human ionizing radiation cancer risk was not scientifically justifiable. The reason(s) for this omission have never been probed in the literature.

The timing of the 1972 BEIR Report [5] was also critical, coming just two years after the creation of EPA. The 1972 BEIR Report indicated (page 51) that one of its principal goals was to provide EPA with the scientific basis for estimating risks at low levels of radiation exposure. In fact, in 1975 the EPA [1] announced that it was basing its cancer risk assessment upon the recommendations of the 1972 BEIR Report [5] with emphasis on the Russell et al. dose rate findings.

This is especially important since the 1972 subcommittee decided to "retain" the linearity recommendation of the 1956 Genetics Panel [3,4] even though the Russell data had shown a clear threshold for ionizing radiation induced mutation for oocytes at some 27,000 fold dose rate greater than background. However, no threshold had been observed for males, even though it was clear that dose rate was predominant and DNA repair was also quite substantial in the males but not quite as active as in the female. It was not known at that time that Russell's findings were in substantial error on the control group background mutation rate for male and female mice. These errors were corrected several decades later by the Russells, revealing that the females displayed an hormetic response whereas the males showed a threshold [15,16].

A principal question then is why didn't the 1972 BEIR I [5] Genetics Subcommittee address the convergent significant uncertainty conclusions of the 1960 BEAR Genetics and Medical Panels [2]. Since Crow was a member of all past Genetics committees/panels and chair of the 1962 Genetics Panel he had strong historical knowledge and context. Crow would also become an "unofficial" historian for the genetics community with many historical reflections. Thus, Crow would have had the historical presence and respect for such prior activities.

In 1960 it was known that dose rate was a central concept in genetics and that male and female mouse reproductive cells could repair mutations. Thus, the geneticist dogma of 1956 that all mutation damage was cumulative, non-reparable and irreversible had been effectively challenged and found to be largely incorrect by Russell. Also,

other examples of ionizing radiation thresholds for mutation had been reported for other biological models at levels far greater than background doses [8,17].

4. A nascent EPA adopts LNT

These developments had the potential to suggest that a threshold model may be biologically more plausible than the LNT. Thus, while the statements of the 1960 BEAR Panels [2] seemed to provide a type of quiet cover or support to the NCRPM policy statement, this veiled support in the form of uncertainty was no longer sufficient (i.e. convincing enough). It is suggested here that the new Congressionally mandated environmental agency, the EPA, created in 1970, needed something better than regulation by uncertainty. The 1972 BEIR Report [5] provided EPA a basis (i.e., male mouse mutagenicity data) to support a linearity approach with the Russell data providing the Gold Standard and could be promoted in public as being based on studies using nearly two million mice. The 1972 BEIR [5] Report had the prerequisite caveats of some uncertainty and erring to some extent on the side of protection. However, the critical point was that now there was sufficient information for a science supported EPA linearity risk assessment policy that would soon have the apparent exacting precision of biostatistical model estimates of cancer risks in the low dose zone via the LNT approach. This historical evaluation suggests that the EPA did not want to have its hands tied or its scientific image affected by statements from the 1960 BEAR Genetics and Medicine Panels [2] that there was too much uncertainty to estimate cancer risk in the low dose zone. Their comments were simply ignored and swept under the regulatory rug.

Funding

This research received no specific grant from any funding *agency in the public, commercial, or not-for-profit sectors.* EJC acknowledges longtime support from the U.S. Air Force (AFOSR FA9550-13-1-0047) and ExxonMobil Foundation (S18200000000256). The views and conclusions contained herein are those of the author and should not be interpreted as necessarily representing policies or endorsement, either expressed or implied. Sponsors had no involvement in study design, collection, analysis, interpretation, writing and decision to and where to submit for publication consideration.

Declaration of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cbi.2019.05.027.

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